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TANAFFOS

Comparison of the Serum Electrolyte Levels among Patients Died and Survived in the Intensive Care Unit

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Background: This study aimed to evaluate the prevalence of serum sodium and potassium disorders and assess their effects on mortality rate in hospitalized patients in the ICU and also to identify prognosis and predictors of survival.

Materials and Methods: A retrospective case-control study was conducted on 457 hospitalized patients in the ICU of Rasoul-e-Akram Hospital (Tehran, Iran). There were two groups: 239 patients who died in the ICU(cases) and 218 patients who were discharged from the ICU(controls). Normal serum concentrations of sodium and potassium were considered as 135-150 and 3-5.5 mEq/L, respectively. Data were analyzed using Chi square test, Independent t-test, One Way ANOVA, Correlation and Receiver Operating Characteristic (ROC) curve.

Results: The mean serum sodium concentration in patients who died and discharged patients was 137.56(SD=8.56) and 137.17(SD=5.11) mEq/L, respectively. Whereas, hyponatremia was significantly more common in expired patients (39.7% vs. 28%, $P<0.001$). On the other hand, the mean serum potassium concentration in expired and discharged patients was 4.42(SD=0.90) and 4.16(SD=0.59)mEq/L, respectively. Hyperkalemia was significantly more common in expired patients (9.2% vs. 0.9%, $P<0.001$). There was a significant negative correlation between serum sodium concentration and patient's age ($P=0.029$, R Spearman = - 0.123). In addition, ROC analysis showed that serum potassium concentration could potentially be a predictor of death in ICU patients ($P=0.003$, Area Under Curve (AUC) = 0.581).

Conclusion: Hyponatremia and hyperkalemia are highly prevalent in expired ICU patients which is compatible with the findings of some other studies. Mortality of ICU patients is linked, in greater part, to organ dysfunction, but the severity of serum sodium and potassium disturbances remains a significant predictor of mortality. Thus, correcting electrolyte disturbances in ICU patients is important.

Key words: Intensive care unit (ICU), Mortality, Electrolyte disturbance, Sodium, Potassium

INTRODUCTION

Intensive care unit (ICU) services require expensive technology, and account for as much as 10 percent of all health care costs. The outcome of critically ill patients is therefore of importance not only to the patients and their families, but also to the society. After admission to the ICU, the outcome is dependent upon both the diagnosis and management of the primary illness and, in many cases, the presence or absence of multi-organ involvement (1).

On the other hand, electrolytes such as potassium, sodium, magnesium, calcium and phosphate play important roles in cellular metabolism and energy

transformation, and in the regulation of cell membrane potentials, especially those of muscle and nerve cells, which demonstrate their important role in the outcome of critically ill patients. Depletion of these electrolytes can induce a wide range of clinical disorders, including neuromuscular dysfunction and severe arrhythmias. The risk for these disorders increases significantly when more than one electrolyte is deficient (2).

It is well known that hypokalemia can induce cardiac arrhythmias (especially in patients with ischemic heart disease and left ventricular hypertrophy), and that it is associated with other adverse effects such as muscle weakness, rhabdomyolysis, renal failure and hyperglycemia. Additionally, hyperkalemia may cause symptoms such as severe muscle weakness or paralysis and cardiac conduction abnormality which may lead to adverse outcomes in ill ICU patients (3-6).

Moreover, hyponatremia is a common electrolyte abnormality in critically ill patients (6-9). The risk of hyponatremia among hospitalized patients is influenced by the underlying disease state and clinical circumstances. The symptoms directly attributable to hyponatremia primarily occur with acute and marked reductions in the plasma sodium concentration and reflect neurologic dysfunction induced by cerebral edema. In this setting, the associated fall in plasma osmolality creates an osmolal gradient that favors water movement into the cells, leading in particular to brain edema (6,10,11). Another sodium disturbance, hypernatremia, is basically a mirror image of hyponatremia (6,10-12). The rise in the plasma sodium concentration and osmolality causes acute water movement out of the brain; this decrease in brain volume can cause rupture of the cerebral veins, leading to focal intracerebral and subarachnoid hemorrhages and possible irreversible neurologic damage. The clinical manifestations of this disorder begin with lethargy, weakness, and irritability, and can progress to twitching, seizures, and coma (6, 10).

Thus, the importance of regulating potassium and sodium levels is well recognized in most intensive care units (ICUs). On the other hand, the development of many electrolyte disturbances in the ICU can be prevented by attention to the usual intravenous fluids and nutrition. Most studies on this subject are focused on the incidence and prevalence of these electrolyte disturbances among ICU patients. Therefore, the aim of this study was to evaluate the prevalence of serum sodium and potassium disorders in order to assess their effects on mortality rate in ICU and identify predictors of prognosis of ICU patients.

MATERIALS AND METHODS

This retrospective case-control study was performed on 457 patients who were hospitalized in the intensive care unit (ICU) of Rasoul-e-Akram Hospital in Tehran, Iran. They were divided into two groups: 239 patients who expired in the ICU (cases) and 218 patients who were discharged from the ICU (controls).

It should be mentioned that, only patients with internal medical problems who were admitted to the medical ICU were studied and patients undergoing nonelective (emergency) or elective surgical procedures were not included in the present study.

Demographic and clinical data were collected for all patients including: age, sex and etc. Additionally, laboratory data such as potassium and sodium serum concentrations were recorded. Normal serum concentrations of sodium and potassium were considered as 135-150 mEq/L and 3-5.5 mEq/L, respectively. Lower levels were used as the cutoff points for clinically significant electrolyte depletion, and the upper levels as cutoff points for significant increase in electrolyte concentration.

The outcome of patients' admission to the ICU was also derived from their medical records and documents including: death or discharge.

Data were analyzed using SPSS version 13.5 software. All data were expressed as mean ±SD. The distribution of nominal variables was compared using Chi-squared test. In order to compare the mean values of quantitative variables the independent t-test and One Way ANOVA were used. To better assess the factors related to the outcome of ICU admission, Correlation and Receiver Operating Characteristic (ROC) curve analyses were performed. Multivariate analysis was also used to evaluate the independency of the effect of meaningful factors. A two-sided p-value<0.05 was considered to be statistically significant.

RESULTS

A total number of 457 patients were included in our study with a mean age of 60.19(SD=19.91) years. They were divided into two groups: 239 patients who expired in the ICU (cases) and 218 patients who were discharged from the ICU (controls).

In the case group, there were 98(41%) females and 141(59%) males with a mean age of 62.85(SD=19.03) years (range 2-107 years). In the control group, 93 (42.7%) females and 125(57.3%) males were studied with a mean age of 57.28(SD=20.48) years (range 2-104 years).

The results are summarized in Table 1. As it is shown, the mean value of serum sodium level was 137.56(SD=8.46) mEq/L and 137.17(SD=5.11) mEq/L, in expired and discharged patients, respectively. Independent t-test demonstrated that this difference was not statistically significant (P=0.546). Whereas, while evaluating serum sodium status qualitatively with Chi^2 test, it was revealed that hyponatremia was significantly more common in expired patients (39.7% vs. 28%, P<0.001). Hypernatremia was also significantly more common in expired patients (6.3% vs. 0.5%, P<0.001). Qualitative evaluation of serum sodium status in the two groups is illustrated in Figure 1.

The mean value of serum potassium concentration in expired and discharged patients was 4.42(SD=0.90) *mEq/L* and 4.16(SD=0.59) *mEq/L*, respectively. This difference was shown to be statistically significant by the independent t-test (P<0.001). In addition, evaluating serum potassium status qualitatively with Chi^2 test also showed that hyperkalemia was significantly more common in expired patients (9.2% vs. 0.9%, P<0.001). Qualitative evaluation of serum potassium status in the two groups is illustrated in Figure 2.

Table 1. Demographic characteristics and main clinical variables of patients in the two groups

Variable	CASE Expired patients (n=239)	CONTROL Discharged patients (n=218)
Age (year) *mean±SD*	62.85±19.03	57.28±20.48
Gender %		
Female	98(41%)	93(42.7%)
Male	141(59%)	125(57.3%)
Serum Sodium level (mEq/L) *mean±SD*	137.56±8.46	137.17±5.11
Serum Potassium level (mEq/L) *mean±SD*	4.42±0.90	4.16±0.59
Serum Sodium status %		
Hyponatremia	95(39.7%)	61(28%)
Normal	129(54%)	156(71.5%)
Hypernatremia	15(6.3%)	1(0.5%)
Serum Potassium status %		
Hypokalemia	11(4.6%)	7(3.2%)
Normal	206(86.2%)	209(95.9%)
Hyperkalemia	22(9.2%)	2(0.9%)

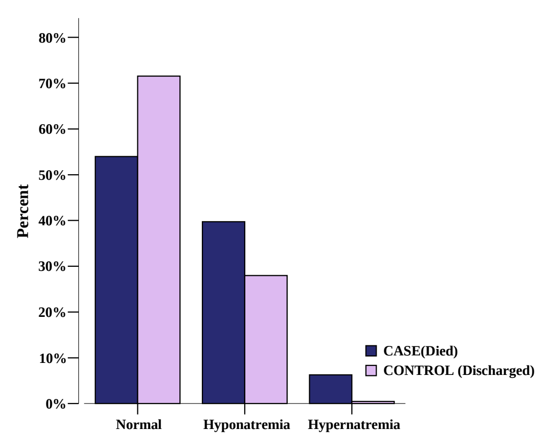

Figure 1. Prevalence of different serum sodium conditions among patients in the two groups (P<0.001).

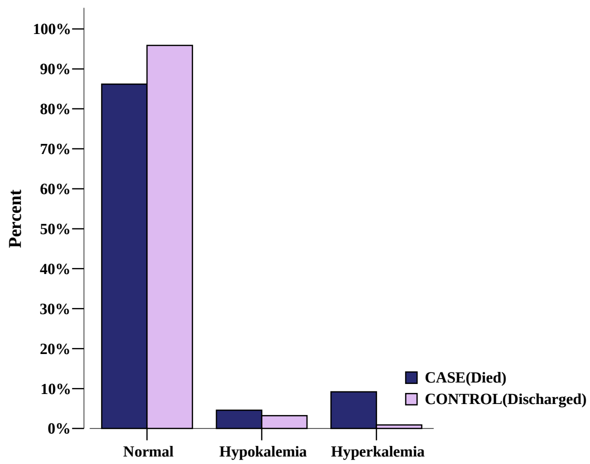

Figure 2. Prevalence of different serum potassium conditions among patients in the two groups of study (P<0.001)

There was a significant negative correlation between serum sodium concentration and patients' age (P=0.029, $R_{Spearman} = -0.123$). However, multivariate analysis showed that the effect of serum sodium qualitative status on the patients' outcome was independent from age (P<0.001).

In addition, ROC analysis showed that serum potassium concentration could potentially be a predictor of death in ICU patients (P=0.003, Area Under the Curve (AUC) = 0.581), while this correlation was not significant for serum sodium level (P = 0.489, AUC = 0.481). Results of ROC curve analysis are shown in Figure 3.

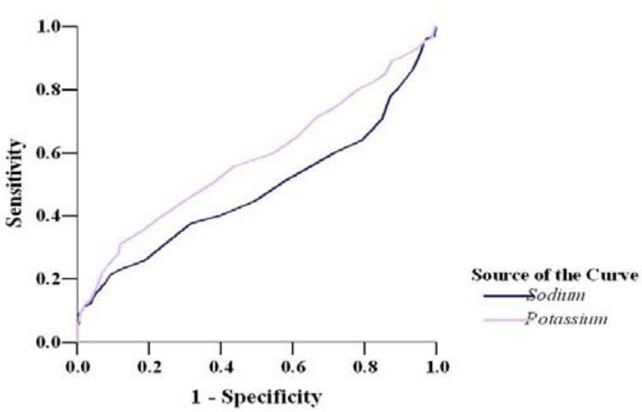

Figure 3. Comparison of ROC for serum Sodium and Potassium level to predict death in patients admitted to the ICU (Serum Potassium: P = 0.003, AUC = 0.581 vs. serum Sodium: P = 0.489, AUC = 0.481)

DISCUSSION

Electrolyte monitoring of patients especially those in the intensive care unit (ICU) is of great importance. There are many studies that have evaluated serum electrolytes of hospitalized patients.

A study was performed by Whelan et al in order to evaluate serum sodium as a risk factor for in-hospital mortality in acute unselected general medical patients and all emergency medical patients admitted to a hospital linked to the patient administration system and laboratory datasets. The serum sodium was measured at admission in all cases where it was deemed clinically necessary. A total of 14,239 patients (47.5% male) were evaluated. Mortality rate was the highest in patients whose sodium level was <125 or >140 mmol/L. The unadjusted OR of death within 30 days of admission was 3.36 and 4.07 with sodium level <125 and >140 mmol/L, respectively. The association between hyponatraemia and mortality remained significant after adjustment for acute illness score, age, sepsis, ICU admission and blood transfusion requirement, which are all powerful predictors of in-hospital mortality. This finding suggests that hyponatremia per se is responsible for a number of in-hospital deaths (13).

In a systematic review in 2012 on prevalence of hyponatremia in geriatric wards compared to other settings over four decades, 53 studies were evaluated. Prevalence of hyponatremia was stable from 1976 to 2006, and higher in geriatric wards. Prevalence of mild hyponatremia (serum sodium <135mM) was 22.2% in geriatric wards, 6.0% in other hospital wards and 17.2% in one ICU-study; prevalence of severe hyponatremia (serum sodium<125mM) in the mentioned settings was 4.5%, 0.8% and 10.3% respectively. In nursing homes prevalence of mild hyponatremia was 18.8% (9).

Hawkins (14) analyzed a large database of >300,000 sodium samples spanning a 2-year period on more than 120,000 patients treated at a 1,200-bed acute care hospital and its attendant ambulatory hospital- and community-based clinics in Singapore. The distribution of patients in

this study was as follows: 36% acute hospital care, 44% ambulatory hospital care, and 20% community-based care. In the acute hospital care group, hyponatremia (serum sodium <136 mEq/L) was observed in 42.6% of the patients. Values <126 mEq/L and <116 mEq/L were noted in 6.2% and 1.2% of the patients, respectively. Similarly, Hoorn and colleagues (15) reported, in abstract form, the results of a 3-month prospective cohort study of 2,907 patients hospitalized at the Erasmus Medical Center in Rotterdam; the incidence of hyponatremia (serum sodium <136 mEq/L) was approximately 30%. Values of ≤125 mEq/L were observed in 2.6% of the patients.

A defect of water excretion can develop or worsen during the course of hospitalization as a result of several antidiuretic influences (e.g., medications, pain, severe nausea, organ failure) (16). Such a defect can generate or aggravate hyponatremia if coupled with the intake of electrolyte-free water in amounts exceeding the capacity for water excretion plus insensible losses. In a subgroup analysis of hospitalized patients with moderate-to-severe hyponatremia (serum sodium ≤125 mEq/L), Hoorn and coworkers (15) found that hospital-acquired hyponatremia (i.e., admission serum sodium >136 mEq/L) and hospital-aggravated hyponatremia (i.e., admission serum sodium 126 to 136 mEq/L) were present in 16% and 46% of patients, respectively. In the large acute hospital care group reported by Hawkins (14), 28.2% and 14.4% of the patients manifested admission and hospital-acquired hyponatremia (serum sodium <136 mEq/L), respectively. The variable proportion of hospital-acquired hyponatremia reported in various studies might reflect a number of factors, including differences in case mix and severity of hyponatremia. For example, in the Hawkins study (14), the proportion of patients with hospital-acquired hyponatremia was much higher in the group with moderate-to-severe hyponatremia than in patients with hyponatremia overall.

Beyond all these studies, different studies define hyponatremia by different values. However, for the purposes of this discussion, hyponatremia predominantly reflects a serum sodium level of <135 mEq/L (17). In addition, the risk for hyponatremia among hospitalized patients is influenced by the underlying disease state and clinical circumstances (18).

Our study is one of the first to evaluate the effect of this electrolyte disturbance on patients' outcome in the ICU. Although using different reference values, the results of our study also show that hyponatremia (serum sodium level of <135 mEq/L) was significantly more common among ICU-admitted patients who expired. Previously, the independent effect of hyponatremia was also demonstrated in hospitalized cirrhotic patients, and the authors concluded that it is a significant factor for mortality of cirrhotic patients (19), similar to what we found in ICU-admitted patients.

This study had some limitations. It was not designed to include details of underlying diseases or patients' medication history but clearly, the inclusion of such information may help to find an explanation for the cause of electrolyte abnormalities in some cases.

Another study showed that the development of hypernatremia is associated with adverse outcomes for patients developing hypernatremia in the ICU and hypernatremia could potentially be used as an indicator of quality of care in the medical ICU (20). In our study, hypernatremia was also more frequent in ICU-admitted patients who expired; but, it was not as frequent as hyponatremia.

Potassium disturbance is one of the most frequent electrolyte abnormalities encountered in the ICU patients. As individuals obtain potassium from their diet, and because many ICU patients are fasting, hypokalemia is a frequent concern. Moreover, hypokalemia is a multifactorial and usually hospital-acquired condition associated with hyponatremia and

hypomagnesaemia. One out of every six patients with hypokalemia develops subsequent hyperkalemia.

The importance of regulating potassium levels is well recognized in most intensive care units (ICUs) and potassium levels are measured frequently, especially in patients with cardiovascular disease.

In a recent study by Crop et al, from 1,178 patients in whom serum potassium level was measured, 140 patients (12%) with hypokalemia were identified and also 23 patients (16%) developed hyperkalemia (21).

In our study, the mean value of serum potassium level was significantly higher in ICU-admitted patients who died and it was showed that serum potassium concentration could potentially be a predictor of death in ICU patients. Moreover, both hyperkalemia and hypokalemia were more frequently seen in expired patients; although, the difference was more significant for hyperkalemia (9.2% vs. 0.9%) than hypokalemia (4.6% vs. 3.2%).

CONCLUSION

The results of our study show high prevalence of hyponatremia and hyperkalemia in expired ICU patients which is confirmed by some other studies as well. Mortality of ICU patients is linked, in greater part, to organ dysfunction, but the severity of serum sodium and potassium concentrations remains a significant predictor of mortality. Thus, correcting electrolyte disturbances in ICU patients is a necessity. Repeated electrolyte measurements are recommended after initial correction to ensure appropriate electrolyte supplementation during the patients' ICU admission in order to decrease ICU mortality rate.

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